REMARKS

The Office Action mailed December 19, 2001 has been received and reviewed. Claims 1-17 and 19-22 are pending in the application. All claims stand rejected. Applicants propose to amend claims 19 and 22 as set forth herein. All amendments are made without prejudice or disclaimer. Reconsideration is respectfully requested.

I. 35 U.S.C. § 112, Second Paragraph

Claim 22

Claim 22 was rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention. Applicants propose to amend claim 22, and in view of the proposed amendment respectfully traverse the rejection.

Applicants propose to amend claim 22 to recite "the population is a cell line." "Population" is defined in the specification to include cell lines. (*See* Specification (as filed), page 13, lines 19-20.) Therefore, applicants request that the 35 U.S.C. § 112, second paragraph, rejection be withdrawn.

II. 35 U.S.C. § 103(a)

A. Claims 1-3, 7, 9-11, 19, 20, and 22

Claims 1-3, 7, 9-11, 19, 20, and 22 were rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Dellaporta and Koes et al. Applicants respectfully traverse the rejections.

With respect to independent claims 1 and 19, and the claims depending therefrom, the Office asserts that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to have used the DNA pooling method of Koes et al. in the insertion element screening method of Dellaporta." (Office Action, page 4). However, at the time of the invention, there was no reasonable expectation of success to combine Dellaporta and Koes et al. as suggested by the Office.

The use of the screening method described in Dellaporta is dependent on the sensitivity by which one sequence can be detected in a mixture of pooled DNA sequences. The non-selective PCR

amplification in Dellaporta may decrease the sensitivity of the screening method because some sequences may replicate less efficiently, making the sequences underrepresented in the sample. Thus, the more complex the mixture of pooled DNA sequences, the higher the risk that the sequence will be underrepresented and not detected. As known to those of ordinary skill in the art, in a non-selective amplification of a mixture of 30 sequences, some sequences may be far overrepresented and some sequences may be far underrepresented or nearly out titrated. After amplification, some sequences may be present at a ratio of only 1 to 300 or less, instead of 1 to 30 resulting in the underrepresented sequences potentially not being detectable in the subsequent hydridization assay as disclosed in Dellaporta.

As stated in Dellaporta, the screening method requires a large number of "insertional mutagens which are capable of producing large numbers of mutations both within individuals and populations, thereby increasing the effective number of mutations which may be obtained and subsequently screened" such that a high probability of identifying a mutant for any given locus will exist. (*See* U.S. Patent 6,013,486, Col. 3, lines 54-58 and Col. 4, lines 31-34). Therefore, the screening method of Dellaporta is limited to a simple array because a large number of insertional mutants is required for efficient screening of the pool, wherein a complex three dimensional array would be unsuitable.

This situation is in contrast to the screening method disclosed in Koes et al. which uses a three-dimensional pool and gene-specific primers. (*See*, Koes et al., Abstract). Since Koes et al. uses gene-specific primers, the more complex three-dimensional array may be efficiently screened for mutants. Furthermore, the disclosure in Koes et al. is limited to screening for insertion mutants in **specific** genes of petunia plants because defined insertion sequences are required (*See*, Koes et al. p. 8152), while Dellaporta is designed to screen for insertional mutants for **any given locus** in a population (*See* U.S. Patent 6,013,486, Col. 3, lines 47-57). Therefore, it would not have been evident to one of ordinary skill in the art to combine Dellaporta and Koes et al.

Also, no suggestion or motivation exists in Dellaporta to combine the screening method with a three-dimensional pooling method, and Koes et al. does not suggest or motivate combining the three-dimensional pooling method with the screening method. In light of the foregoing, applicants respectfully submit that combining Dellaporta with Koes et al. is not proper, that a *prima facie* case

of obviousness has not been shown, and that the rejections be withdrawn with regard to claims 1-3, 7, 9-11, 19, 20, and 22.

With further regard to claim 19, applicants propose to amend the claim to limit the nucleic acid to which the labelled amplification products will hydridize to a gene library. In view of the proposed amendment and the above analysis, applicants respectfully request reconsideration and withdrawal of the rejection of claim 19.

B. Claim 4

Claim 4 was rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Dellaporta and Koes et al. as applied to claims 1-3, and further in view of Sour et al. Applicants respectfully traverse the rejection.

Claim 4 is allowable at the very least as depending from non-obvious independent claim 1.

Furthermore, a *prima facie* case of obviousness has not been set forth by the Office with respect to claim 4. As admitted by the Office, "[n]either Dellaporta nor Koes et al. teach reamplifying at least one amplifiable genomic fragment with at least one primer based on a sequence of a nucleic acid insertion element." (Office Action, page 4). Furthermore, Sour et al. does not suggest or motivate the use of the three-dimensional array or the screening method as disclosed in Dellaporta and Koes et al. Therefore, applicants respectfully submit that a *prima facie* case of obviousness has not been shown with regard to claim 4, and request reconsideration and withdrawal of the obviousness rejection.

C. Claims 5, 6, 8, and 12

Claims 5, 6, 8, and 12 were rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Dellaporta and Koes et al. as applied to claim 1, and further in view of Vos et al. Applicants respectfully traverse the rejections.

Claims 5, 6, 8, and 12 are allowable at the very least as depending from non-obvious independent claim 1.

Furthermore, neither Dellaporta nor Koes et al. teach amplification by transposan display amplification (*See* Office Action, page 5) and Vos et al. does not suggest or motivate the use of a

screening method or three-dimensional array. Therefore, a *prima facie* case of obviousness has not been set forth by the Office with respect to claims 5, 6, 8, and 12. Accordingly, applicants request reconsideration and withdrawal of the rejections.

D. Claims 13-17 and 21

Claims 13-17 and 21 were rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Dellaporta and Koes et al. as applied to claims 1 and 19. Applicants respectfully traverse the rejections.

Claims 13-17 and 21 are allowable at the very least as depending from non-obvious independent claims 1 and 19, respectively.

The Office states that "reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time of the invention." (Office Action, page 7). However, as stated by the Federal Circuit "[t]he mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior also suggests the desirability of the combination." (Emphasis in original) *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) and M.P.E.P. § 2143.01. Since neither Dellaporta nor Koes et al. suggest the use of kits, the Office has not set forth a *prima facie* case of obviousness with regard to claims 13-17 and 21. Therefore, applicants respectfully request reconsideration and withdrawal of the obviousness rejections.

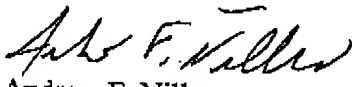
ENTRY OF AMENDMENTS

The proposed amendments to claims 19 and 22 should be entered by the Examiner because the amendments are supported by the as-filed specification and drawings and do not add any new matter to the application. Further, the amendments do not raise new issues or require a further search. Finally, if the Examiner determines that the amendments do not place the application in condition for allowance, entry is respectfully requested since they certainly remove issues for appeal.

CONCLUSION

In view of the amendments and remarks presented herein, applicants respectfully submit that the amended claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Attachment: Marked up version of the amended claims

VERSION WITH MARKINGS TO SHOW CHANGES MADE

19. (Thrice Amended) A method for parallel simultaneous screening for one or more gene insertion mutants in a population of any organism comprising:

preparing an insertion element mutant library comprising a plurality of nucleic acid insertion elements and insertion element flanking sequences, said insertion element flanking sequences originating from a defined population of an organism wherein said gene insertion mutants are to be detected and wherein said insertion element library is built in a 3D-array of block, row and column pools;

amplifying said insertion element flanking sequences from said insertion element mutant library using at least one primer derived from a sequence of a nucleic acid insertion element of said plurality of nucleic acid insertion elements; and

producing a set of labelled amplification products representing said insertion element flanking sequences derived from said block, row and column pools to use as probes to hybridize to a solid support to which [one or more nucleic acids] a gene library [have] has been fixed as target(s) for hybridisation, wherein said gene library is organized in at least a two-dimensional array.

22. (Amended) The method according to claim 1 wherein the [organism] population is a cell line.